



# Type 2 Diabetes

A VA Clinician's Quick Reference  
Guide to Diabetes Management  
in Primary Care (2020)

**VA**



**U.S. Department of Veterans Affairs**

Veterans Health Administration  
*PBM Academic Detailing Service*



# Type 2 Diabetes

A VA Clinician's Quick Reference  
Guide to Diabetes Management  
in Primary Care (2020)

**VA**



**U.S. Department of Veterans Affairs**

Veterans Health Administration  
*PBM Academic Detailing Service*

## Contents

Abbreviations.....	2	Combining diabetes agents.....	16
Diagnosing prediabetes and type 2 diabetes .....	3	Basal insulin initiation.....	17
Important considerations for the HbA1c test.....	4	Hypoglycemia .....	18
HbA1c targets.....	5	Adding prandial insulin .....	19-20
Algorithm for initiating and advancing pharmacotherapy for type 2 diabetes.....	7	Sample day with basal and prandial insulin .....	21
Select pharmacotherapy based on Veteran characteristics .....	8-11	Visit planning guide .....	22-26
Renal dosing for glucose-lowering medications .....	12-15	Resources .....	27
		References .....	28-29

## Abbreviations

**ASCVD:** atherosclerotic cardiovascular disease

**BG:** blood glucose

**CKD:** chronic kidney disease

**COPD:** chronic obstructive pulmonary disease

**CVD:** cardiovascular disease

**dL:** deciliter

**DPP-4:** dipeptidyl peptidase-4

**eGFR:** estimated glomerular filtration rate

**FPG:** fasting plasma glucose

**FIB:** fibrosis

**G6PD:** glucose-6-phosphate dehydrogenase

**GI:** gastrointestinal

**GLP-1:** glucagon-like peptide-1

**gm:** gram

**HbA1c:** hemoglobin A1c

**HF:** heart failure

**kg:** kilogram

**LVH:** left ventricular hypertrophy

**mcg:** microgram

**MEN2:** multiple endocrine neoplasia syndrome type 2

**mg:** milligram

**MTC:** medullary thyroid carcinoma

**NYHA:** New York Heart Association

**SGLT-2:** sodium glucose co-transporter-2

**TZD:** thiazolidinediones

**UACR** urine albumin-to-creatinine ratio

**UTI:** urinary tract infection

**XR:** extended release

## Diagnosing prediabetes and type 2 diabetes:<sup>1</sup>

Status	Fasting Plasma Glucose (FPG)* <sup>§</sup> or Hemoglobin A1c (HbA1c) <sup>±</sup>
Normal	FPG < 100 mg/dL; HbA1c < 5.7%
Prediabetes	FPG ≥ 100 mg/dL and < 126 mg/dL on 2 occasions <b>or</b> HbA1c ≥ 5.7% and FPG ≥ 100 mg/dL and < 126 mg/dL <b>or</b> 2-hour plasma glucose 140 - 199 mg/dL (IGT)
Diabetes	FPG ≥ 126 mg/dL on 2 occasions <b>or</b> HbA1c ≥ 6.5% and a confirmatory FPG ≥ 126 mg/dL <b>or</b> HbA1c ≥ 7.0% on 2 occasions

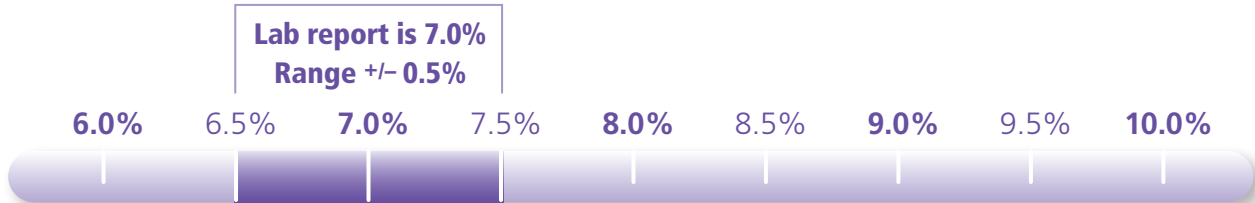
\*Fasting is defined as no caloric intake for at least 8 hours. <sup>§</sup> FPG is the preferred test for diagnosis, but either of the two listed tests is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these two tests should be done on different days. <sup>±</sup> Using a clinical laboratory (not a point-of-care) methodology standardization to the National Glycohemoglobin Standardization Program (NGSP).

IGT: impaired glucose tolerance during oral glucose tolerance test (OGTT).

See the *VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care (2017)* for more information.

## Important considerations for the HbA1c test<sup>2</sup>

- Reliability of HbA1c measurements depend on the lifespan of red blood cells.
- High red blood cell turnover such as in hemolytic anemia, acute blood loss, erythropoietin treatment, and dialysis can all result in falsely low HbA1c.
- Low red blood cell turnover, such as in vitamin deficiencies and chronic kidney disease, can result in a falsely high HbA1c.
- In these cases, an FPG or an oral glucose tolerance test (OGTT) are preferred for diagnosis.
- A single HbA1c measurement should be thought of as a range and not an absolute value. Therefore, an HbA1c of 7.0% could be anywhere in the range of 6.5 to 7.5%. This is due to the accuracy of the laboratory test. Keep this in mind when determining an HbA1c target range for a patient and if adjustments in therapy are needed.



## HbA1c targets

Individual target ranges may vary based on clinical judgment and Veteran preferences. Use shared-decision making to help the Veteran explore and compare treatment options to determine their optimal care plan.

### Selecting and adjusting an HbA1c treatment target<sup>2</sup>

Major comorbidities <sup>1</sup> or physiologic age	Microvascular complications		
	Absent or mild <sup>2</sup>	Moderate <sup>3</sup>	Advanced <sup>4</sup>
<b>Absent*</b> : > 10-15 years of life expectancy	6-7%	7-8%	7.5-8.5%
<b>Present<sup>5</sup></b> : 5-10 years of life expectancy	7-8%	7.5-8.5%	7.5-8.5%
<b>Marked<sup>6</sup></b> : < 5 years of life expectancy	8-9%	8-9%	8-9%

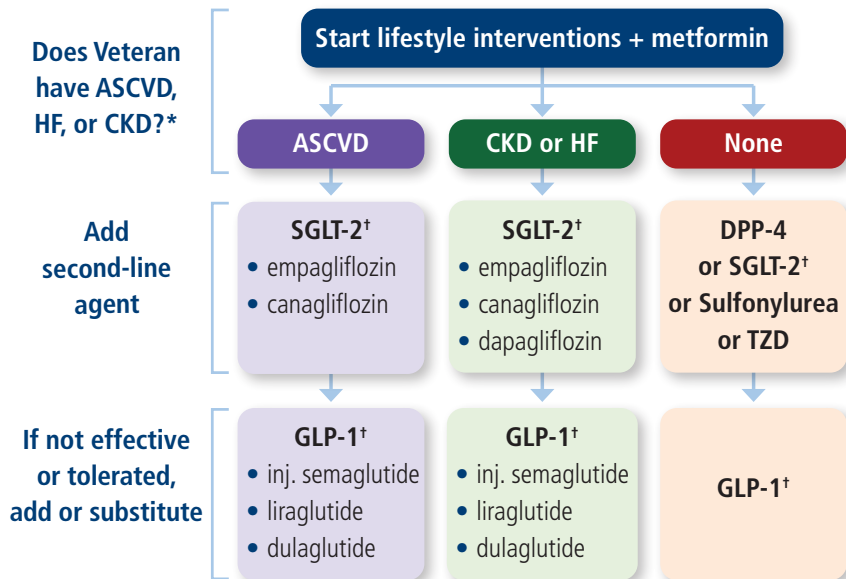
\* Progression to major complications of diabetes is likely to occur in individuals with longer than 15-20 years of life expectancy. Therefore, goal ranges are more beneficial early in disease in younger individuals, or healthier older adults with a longer life expectancy. **The super-scripted numbers in the table above correlate to the comorbidities and microvascular complications listed on Page 6.**

## Comorbidities and microvascular complications *(from previous page)*

- <sup>1</sup> **Major comorbidity:** significant CVD, severe CKD, severe COPD, severe chronic liver disease, recent stroke, and/or life-threatening malignancy
- <sup>2</sup> **Mild microvascular disease:** early background retinopathy, and/or microalbuminuria and/or mild neuropathy
- <sup>3</sup> **Moderate microvascular disease:** pre-proliferative retinopathy or persistent, fixed proteinuria (macroalbuminuria), and/or demonstrable peripheral neuropathy (sensory loss)
- <sup>4</sup> **Advanced microvascular disease:** severe non-proliferative retinopathy, or proliferative retinopathy and/or renal insufficiency (serum creatinine > 2.0mg/dL), and/or insensate extremities or autonomic neuropathy (e.g., gastroparesis, impaired sweating, orthostatic hypotension)
- <sup>5</sup> Major comorbidity is present but is not end-stage and management is achievable.
- <sup>6</sup> Major comorbidity is present and is either end-stage or management is significantly challenging. This can include mental health conditions and substance/opioid use.

**Social determinants** of health, including social support, ability to self-monitor on insulin, food insufficiency, and cognitive impairment need to be considered. Additionally, side effects of medications and patient preferences need to be considered in the process of shared decision making.

# Algorithm for initiating and advancing pharmacotherapy for type 2 diabetes<sup>1</sup>



If HbA1c is > 9%, consider starting basal insulin at any step.

\* **Agents shown to reduce ASCVD risk:** SGLT-2 inhibitors (empagliflozin, canagliflozin); GLP-1 agonists (injectable semaglutide, liraglutide, dulaglutide). GLP-1s have not been shown to lower heart failure risk (neutral outcome). Dapagliflozin has been shown to lower heart failure risk and CKD risk, but neutral for ASCVD.

† **Indicates referral to individual Criteria for Use.**  
Do not combine a DPP-4 inhibitor with a GLP-1 agonist.

Not shown in the figure are uncommonly-used agents (e.g., alpha-glucosidase inhibitors, meglitinides, pramlintide, inhaled insulin, etc.), but these may be considered in specific situations. Refer to Criteria for Use for pramlintide and inhaled insulin: [www.pbm.va.gov](http://www.pbm.va.gov)

**ASCVD:** indicators are age ≥ 55 years with coronary, carotid, or lower extremity artery stenosis > 50% or LVH.

**CKD:** eGFR 30-60 mL/min/1.73m<sup>2</sup> or UACR > 30 mg/g, particularly UACR > 300 mg/g. **HF:** left ventricular ejection fraction < 45%.

## Select pharmacotherapy based on Veteran characteristics<sup>1,4-13</sup>

Class	Medication	HbA1c lowering %	CV outcomes		Renal outcome	Weight change	Hypo-glycemia	Possible side effects/ considerations
			ASCVD	HF				
<b>Biguanide</b>	<b>metformin</b> <b>metformin XR</b>	1-1.5	Possible benefit	*	*	Loss/ Neutral (-1.1 kg)	No	<ul style="list-style-type: none"> <li>• GI side effects common</li> <li>• Risk for B12 deficiency</li> <li>• Lactic acidosis (rare)</li> </ul>
<b>DPP-4 inhibitors</b>	linagliptin sitagliptin	0.5-1	Neutral	Neutral	*	Neutral (-0.4 to 0.55 kg)	No	<ul style="list-style-type: none"> <li>• Pancreatitis</li> <li>• Hypersensitivity reactions</li> <li>• Arthralgias</li> <li>• Bullous pemphigoid</li> </ul>
	<b>alogliptin</b> saxagliptin			Potential risk				

**Formulary medications in bold.** Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: <https://www.pbm.va.gov/PBM/NationalFormulary.asp>.

\*No data available.

Class	Medication	HbA1c lowering %	CV outcomes		Renal outcome	Weight change	Hypo-glycemia	Possible side effects/ considerations
			ASCVD	HF				
GLP-1 receptor agonists	<b>inj. semaglutide</b> <b>liraglutide</b> dulaglutide	1-1.5	Benefit	Neutral	Benefit	Loss/ (-0.28 to 3.2 kg) <sup>†</sup>	No	<ul style="list-style-type: none"> <li>• Contraindicated in those with personal or family history of MTC or those with MEN2</li> <li>• GI side effects common</li> <li>• Possible pancreatitis</li> <li>• Hypersensitivity</li> <li>• Immunogenicity</li> <li>• Acute kidney injury</li> </ul>
	exenatide lixisenatide oral semaglutide		Neutral	Neutral	*			

† Semaglutide injection appears to produce the most weight loss among the GLP-1 agonists.

## Select pharmacotherapy based on Veteran characteristics<sup>1,4-13</sup>

Class	Medication	HbA1c lowering %	CV outcomes		Renal outcome	Weight change	Hypo-glycemia	Possible side effects/ considerations
			ASCVD	HF				
<b>SGLT-2 inhibitors</b>	<b>empagliflozin</b> canagliflozin	0.5-1 <sup>±</sup>	Benefit	Benefit	Benefit	Loss (-1.8 to 3.3 kg)	No	<ul style="list-style-type: none"> <li>• Genital mycotic infections</li> <li>• UTI</li> <li>• Ketoacidosis</li> <li>• Volume depletion</li> <li>• Acute kidney injury</li> <li>• Fournier's Gangrene</li> <li>• Bone fractures (canagliflozin)</li> <li>• Amputation (canagliflozin)</li> </ul>
	dapagliflozin		Neutral	Benefit	Benefit			
	ertugliflozin		*	*	*			

**Formulary medications in bold.** \*No data available. \*\*Meta-analysis of short-term trials indicated a potential risk of CV events compared to placebo; however, this was not confirmed in a long-term trial. <sup>±</sup> The effect of SGLT-2 inhibitors in lowering glucose levels is reduced in patients with renal impairment. Despite this, the cardiovascular and renal benefits of SGLT-2 inhibition are maintained to an eGFR as low as 30 mL/min/1.73m<sup>2</sup>.

Class	Medication	HbA1c lowering %	CV outcomes		Renal outcome	Weight change	Hypo-glycemia	Possible side effects/ considerations
			ASCVD	HF				
<b>Sulfonylureas</b>	<b>glipizide</b> <b>glimepiride</b>	1-1.5	Possible harm	*	*	Gain (1-5.5 kg)	Yes	<ul style="list-style-type: none"> <li>• Increased risk of hypoglycemia in elderly or renal impairment</li> <li>• Hemolytic anemia may occur if G6PD deficiency</li> </ul>
<b>TZDs</b>	<b>pioglitazone</b>	1-1.5	Possible benefit	Increased risk	*	Gain (2.6-4.8 kg)	No	<ul style="list-style-type: none"> <li>• Contraindicated in NYHA Class 3 or 4 HF</li> <li>• Bone fractures in women</li> <li>• Edema</li> <li>• Bladder cancer (pioglitazone)</li> </ul>
	rosiglitazone		Possible harm**	Increased risk	*			

## Renal dosing for glucose-lowering medications<sup>1,14-33</sup>

Class	Medication	Starting daily dose	Maximum daily dose	Action if eGFR (mL/min/1.73m <sup>2</sup> )			
				> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD
Biguanide	<b>metformin</b> <b>metformin XR</b>	500 mg BID (IR) or 850 mg daily (IR) or 500mg daily (XR)	2,500 mg (IR) 2,000 mg (XR)	Maximum dose 2,000 mg/day ✓	Do not start; if taking evaluate risk/benefit, reduce dose by 50% with maximum 1,000 mg/day* ••	✗	✗
Sulfonylureas	<b>glipizide</b>	5 mg; 2.5 mg in elderly	40 mg (IR) 20 mg (XR)	2.5 mg/day, slow titration ••	2.5 mg/day, slow titration ••	••	••
	<b>glimepiride</b>	1 – 2 mg	8 mg	1 mg/day, slow titration ••	••	••	✗

\*Monitor renal function more frequently.

Class	Medication	Starting daily dose	Maximum daily dose	Action if eGFR (mL/min/1.73m <sup>2</sup> )			
				> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD
DPP-4 inhibitors	<b>alogliptin</b>	25 mg	25 mg	12.5 mg/day ●●	12.5 mg/day ●●	6.25 mg/day ●●	6.25 mg/day ●●
	linagliptin	5 mg	5 mg	✓	✓	✓	✓
	saxagliptin	2.5 – 5 mg	5 mg	✓	2.5 mg/day ●●	2.5 mg/day ●●	2.5 mg/day ●●
	sitagliptin	100 mg	100 mg	✓	50 mg/day ●●	25 mg/day ●●	25 mg/day ●●
TZD	<b>pioglitazone</b>	15 – 30 mg <sup>§</sup>	45 mg	✓	✓	✓	✓
	rosiglitazone	4 mg	8 mg	✓	✓	✓	✓

**Formulary medications in bold.** <sup>§</sup> Check liver function tests before starting. Use 15mg daily as starting dose if NYHA class 1 or 2.  
**Green (✓):** no adjustment needed; **Yellow (●●):** dose reduction, limited data, or use with caution; dosing guidance provided when available; **Red (X):** avoid or contraindicated.

## Renal dosing for glucose-lowering medications<sup>1,14-33</sup>

Class	Medication	Starting daily dose	Maximum daily dose	Action if eGFR (mL/min/1.73m <sup>2</sup> )			
				> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD
SGLT-2 inhibitors	canagliflozin	100 mg	300 mg	100 mg/day maximum ••	100 mg/day maximum ••	✗	✗
	dapagliflozin	5 mg	10 mg	✓	✗	✗	✗
	<b>empagliflozin</b> ¥	10 mg	25 mg	✓	✓	✗	✗
	ertugliflozin	5 mg	15 mg	✗	✗	✗	✗

**Formulary medications in bold.** **Green (✓):** no adjustment needed; **Yellow (••):** dose reduction, limited data, or use with caution; dosing guidance provided when available; **Red (✗):** avoid or contraindicated.

¥ Note: In EMPA-REG and CREDENCE (canagliflozin), the lower limit for inclusion in the trials was an eGFR of 30mL/min/1.73m<sup>2</sup>. The product labeling for empagliflozin recommends not to initiate empagliflozin if eGFR is less 45 or to discontinue if eGFR falls persistently below 45. The rationale for the labeling is that the glycemic effect is substantially reduced at lower eGFRs.

Class	Medication	Starting daily dose	Maximum daily dose	Action if eGFR (mL/min/1.73m <sup>2</sup> )			
				> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD
GLP-1 receptor agonists	dulaglutide	0.75 mg weekly	1.5 mg weekly	✓	✓	✓	••
	exenatide	10 mcg	20 mcg	Can be used if eGFR 50-80 mL/min/1.73 m <sup>2</sup>	••	✗	✗
	exenatide XR	2 mcg weekly	2 mcg weekly	✓	✗	✗	✗
	<b>liraglutide</b>	0.6 mg	1.8 mg	✓	✓	✓	Limited data ••
	lixisenatide	10 mcg	20 mcg	✓	✓	••	✗
	<b>inj. semaglutide</b>	0.25 mg weekly	1 mg weekly	✓	✓	✓	✓
	oral semaglutide	3 mg	14 mg	✓	✓	✓	✓

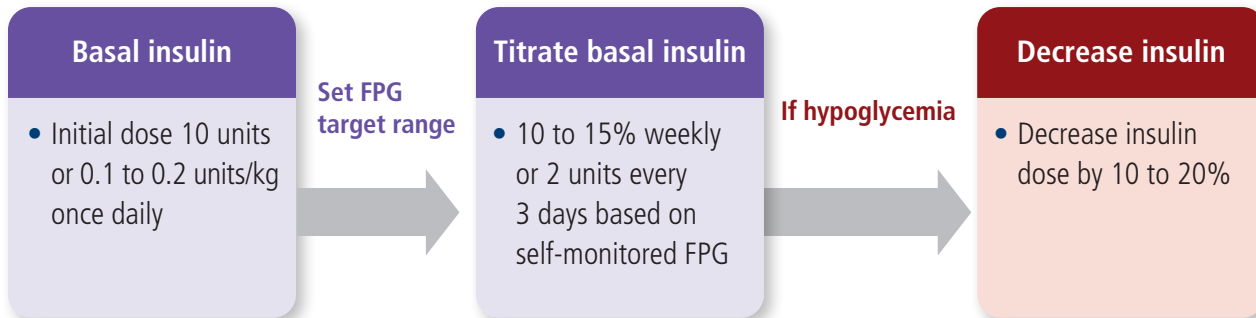
## Combining diabetes agents<sup>1,2</sup>

	DPP-4 inhibitors	GLP-1 agonists	Insulin	Metformin	SGLT-2 inhibitors	SU	TZDs
DPP-4 inhibitors		X	✓	✓	✓	✓	✓
GLP-1 agonists	X		✓*	✓	✓	✓	✓
Insulin	✓	✓*		✓	✓	!	!
Metformin	✓	✓	✓		✓	✓	✓
SGLT-2 inhibitors	✓	✓	✓	✓		✓	✓
SU	✓	✓	!	✓	✓		✓
TZDs	✓	✓	!	✓	✓	✓	

✓: Safe to use together; !: Use with caution. SU + insulin has an increased rate of hypoglycemia, stop SU when prandial insulin used. TZD (pioglitazone) + insulin can cause edema at high insulin doses and in patients with heart failure, avoid using rosiglitazone + insulin.

X: Avoid combining. \*The data for GLP-1 agonists in combination with both basal and prandial insulin or with U500 insulin are very limited at present. Concomitant use of GLP-1 agonists with regimens containing basal insulin AND prandial insulin (including premixed formulations) or with U500 may be done on a case-by-case basis in consultation with an endocrinologist or diabetes specialist.

## Basal insulin initiation\*<sup>1</sup>



\*Individualize insulin regimen based on Veteran-specific factors and glucose measurements.

**Basal insulin:** NPH, detemir, glargine 100μ/mL, and degludec

## Hypoglycemia<sup>1,2</sup>

- Glucose alert value: < 70 mg/dL
- Clinically significant hypoglycemia:  $\leq 54$  mg/dL
- **Severe hypoglycemia:** associated with severe cognitive impairment requiring external assistance for recovery.
- **Treatment:** 15-20 gm glucose or equivalent, recheck BG in 15 minutes and repeat until BG  $\geq 70$ , then have meal or snack to prevent recurrence of hypoglycemia.
- **Severe hypoglycemia treatment:** glucagon emergency kit or IV dextrose by emergency medical services.



### What is 15-20 gm of glucose?

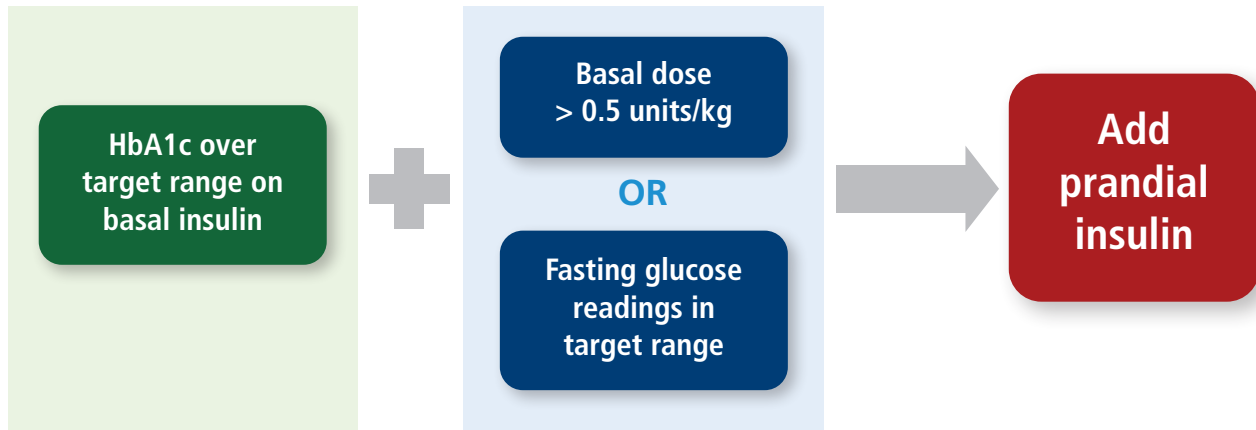
**Glucose tablets or gel can be used.**

Look at label to determine the number of grams. Other sources that can raise blood glucose quickly:

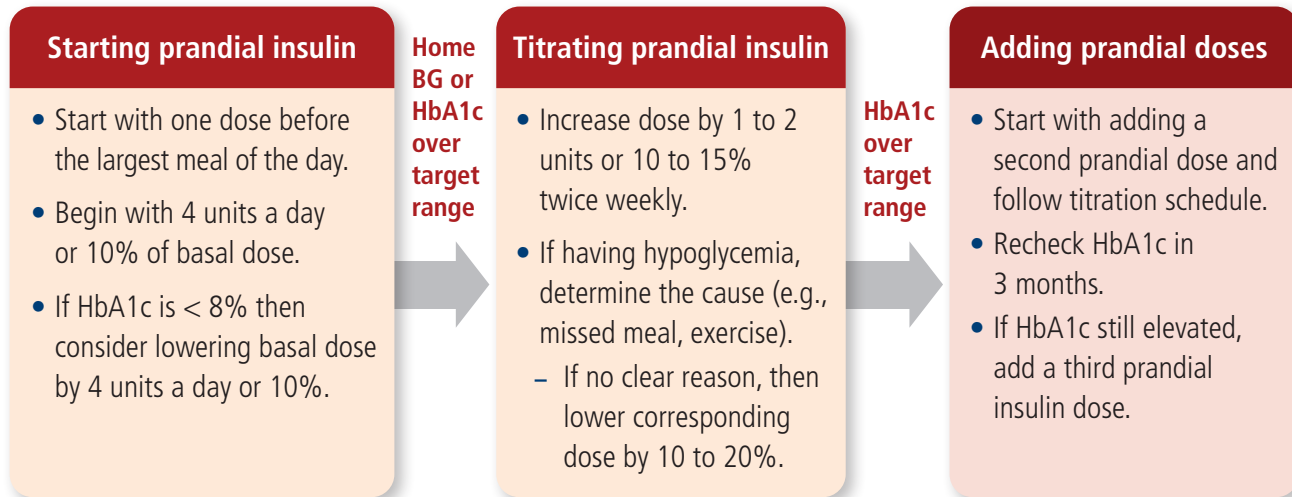
- ✓ 4 ounces (1/2 cup) juice or regular soda
- ✓ 1 tablespoon honey, corn syrup, or sugar
- ✓ 2 tablespoons raisins






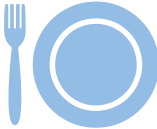




## Adding prandial insulin<sup>1</sup>



## Adding prandial insulin<sup>1</sup> (continued)



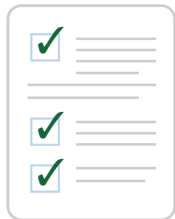
## Sample day with basal and prandial insulin

TIME OF DAY	Morning	Breakfast	Lunch	Dinner
				
INSULIN TYPE	 Basal	 Prandial	 Prandial	 Prandial

\*May need basal insulin two times daily depending on dose and type.

## Visit planning guide<sup>1</sup>

### Past medical and family history



#### Personal history of complications and comorbidities

- Macrovascular and microvascular
- Hypoglycemia (awareness, frequency, causes, timing of episodes)
- High blood pressure or abnormal lipids

Last dental exam

Last dilated eye exam

Visits to specialist

Changes in medical/family history

Follow-up  
visits

Annual  
visit



### Technology use



Glucose monitoring (meter/CGM): results and data use

Follow-up  
visits

Annual  
visit



## Lifestyle factors



Eating patterns and weight history

Physical activity and sleep behaviors

Tobacco, alcohol, and substance use

Follow-up  
visits

Annual  
visit

✓

✓

✓

✓

✓

## Medications and vaccinations



Current medication regimen

Medication taking behavior

Medication intolerance or side effects

Complementary and alternative medicine use

Vaccination history and needs

Follow-up  
visits

Annual  
visit

✓

✓

✓

✓

✓

✓



✓

✓

✓

## Visit planning guide<sup>1</sup>

### Behavioral and diabetes self-management skills

	Follow-up visits	Annual visit
		✓
		✓
	✓	✓
	✓	✓
		✓
	✓	✓

Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted

Consider assessment for cognitive impairment at age 65 or older

History of Medical Nutrition Therapy visit with a dietitian and diabetes self-management education visits/classes

#### Assess for food insecurity:

- In the past 3 months, have you ever run out of food and were not able to access more food or have the money to buy more food?

Assess diabetes self-management skills and barriers

For women of childbearing capacity, review contraceptive needs and preconception planning

## Physical examination



Height, weight, and BMI

Blood pressure measurement

Thyroid palpation

Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)



### **Comprehensive foot examination:**

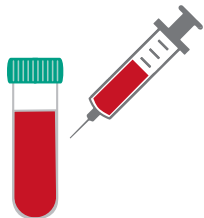
- Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)
- Screen for peripheral arterial disease
- Determination of temperature, vibration, or pinprick sensation, and 10-g monofilament exam

Follow-up visits	Annual visit
✓	✓
✓	✓
	✓
✓	✓
✓*	✓
	✓
	✓

\*Should be performed every visit in Veterans with sensory loss, previous foot ulcers, or amputations.

# Visit planning guide<sup>1</sup>

## Laboratory evaluation



HbA1c, if not available in the past 3 months



Discuss the target HbA1c range with the Veteran



### If not performed/available within the past year:

- Lipid profile, including total, LDL, and HDL cholesterol and triglycerides



- Liver function tests



- Spot urinary albumin-to-creatinine ratio



- Serum creatinine and estimated glomerular filtration rate



- Vitamin B12 if on metformin (when indicated)



- Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics



# Resources

## VA/DoD guides

- **VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care (2017):** [www.healthquality.va.gov/guidelines/cd/diabetes](http://www.healthquality.va.gov/guidelines/cd/diabetes)
- **VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting (2020):** [www.healthquality.va.gov/guidelines/cd/htn/](http://www.healthquality.va.gov/guidelines/cd/htn/)
- **VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease (2019):** [www.healthquality.va.gov/guidelines/cd/ckd/](http://www.healthquality.va.gov/guidelines/cd/ckd/)

## VA programs

- **VA Hypoglycemia Safety Initiative:** [www.qualityandsafety.va.gov/ChoosingWiselyHealthSafetyInitiative/HypoglycemiaSite/Hypoglycemia.asp](http://www.qualityandsafety.va.gov/ChoosingWiselyHealthSafetyInitiative/HypoglycemiaSite/Hypoglycemia.asp)
- **VA PAVE (Prevention of Amputation for Veterans Everywhere):** [www.va.gov/VHAPUBLICATIONS/ViewPublication.asp?pub\\_ID=5364](http://www.va.gov/VHAPUBLICATIONS/ViewPublication.asp?pub_ID=5364)

## Tools/videos

- **How to Give Yourself a Subcutaneous Injection:** [www.youtube.com/watch?v=wXjQHxopzk](http://www.youtube.com/watch?v=wXjQHxopzk)
- **American College of Cardiology ASCVD Plus Tool:** [tools.acc.org/ASCVD-Risk-Estimator-Plus](http://tools.acc.org/ASCVD-Risk-Estimator-Plus)

## References

1. American Diabetes Association, Standards of medical care in diabetes - 2020. *Diabetes Care*, 2020. 43(Suppl 1): p. S1-S207.
2. U.S. Department of Veterans Affairs, U.S. Department of Defense. VA/DoD clinical practice guidelines for the management of diabetes mellitus in primary care. 2017; <https://www.healthquality.va.gov/guidelines/cd/diabetes>. Accessed 25 Jan 2019.
3. Zheng SL, Roddick AJ, Aghar-Jaffar R, et al. Association Between Use of Sodium-Glucose Cotransporter 2 Inhibitors, Glucagon-like Peptide 1 Agonists, and Dipeptidyl Peptidase 4 Inhibitors With All-Cause Mortality in Patients With Type 2 Diabetes: A Systematic Review and Meta-analysis. *JAMA*. 2018;319(15):1580-1591.
4. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med*. 2015;373(22):2117-2128.
5. Pfeffer MA, Claggett B, Diaz R, et al. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. *N Engl J Med*. 2015;373(23):2247-2257.
6. Holman RR, Bethel MA, Mentz RJ, et al. Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med*. 2017;377(13):1228-1239.
7. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med*. 2019;380(4):347-357.
8. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2019;380(24):2295-2306.
9. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med*. 2017;377(7):644-657.
10. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med*. 2016;375(4):311-322.
11. Marso SP, Bain SC, Consoli A, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med*. 2016;375(19):1834-1844.
12. Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet*. 2019.
13. Wanner C, Inzucchi SE, Lachin JM, et al. Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. *N Engl J Med*. 2016;375(4):323-334.
14. Glucophage and Glucophage XR [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2018.
15. Glucotrol (glipizide) [package insert]. New York, NY: Pfizer; 2016.
16. DiaBeta (glyburide) [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; 2016.

17. Amaryl (glimepiride) [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC: 2018.
18. Actos (pioglitazone) [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; 2016.
19. Avandia (rosiglitazone) [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2019.
20. Januvia (sitagliptin) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2018.
21. Onglyza (saxagliptin) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2017.
22. Tradjenta (linagliptin) [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2017.
23. Nesina (alogliptin) [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; 2016.
24. Invokana (canagliflozin) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2018.
25. Farxiga (dapagliflozin) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.
26. Jardiance (empagliflozin) [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2018.
27. Steglatro (ertugliflozin) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2018.
28. Trulicity (dulaglutide) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2019.
29. Bydureon (exenatide extended-release ) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.
30. Byetta (exenatide) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.
31. Victoza (liraglutide) [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; 2017.
32. Adlyxin (lixisenatide) [package insert]. Bridgewater, CT: sanofi-aventis U.S. LLC: 2016.
33. Ozempic (semaglutide) [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; 2017.
34. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-357.



## **U.S. Department of Veterans Affairs**

Veterans Health Administration  
*PBM Academic Detailing Service*

## **U.S. Department of Veterans Affairs**

This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing SharePoint. These are general recommendations only; specific clinical decisions should be made by treating provider based on an individual patient's clinical conditions.

### **VA PBM Academic Detailing Service Email Group:**

PharmacyAcademicDetailingProgram@va.gov

### **VA PBM Academic Detailing Service SharePoint Site:**

<https://dvagov.sharepoint.com/sites/vhaacademicdetailing/SitePages/Home.aspx>

### **VA PBM Academic Detailing Service Public Website:**

<http://www.pbm.va.gov/PBM/academicdetailingservicehome.asp>